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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,600	05/03/2001	Peter Watts	WC 111	9982

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/30/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/848600	Applicant(s) WITTY
	Examiner GAMBEL	Art Unit 1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 4/15/03

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 13-19

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 13-19

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

PAPER NO. 14

DETAILED ACTION

1. Applicant's amendment, filed 4/15/03 (Paper No. 13), has been entered.
Claims 1-5, 7 and 9-12 have been canceled. Claims 6 and 8 have been canceled previously.
Claims 13-19 have been added and are being acted upon presently.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 4/15/03 (Paper No. 13).
The rejections of record can be found in the previous Office Action (Paper No. 12).

3. Newly added claims 13-19 are rejected under 35 U.S.C. § 103 as being unpatentable over Igari et al. U.S. Patent No. 5,482,706; 1449) AND/OR Greve et al. (U.S. Patent No. 5,589,453; 1449) in view of Wegner et al. (U.S. Patent No. 5,730,983; 1449), Gwaltney et al. (U.S. Patent No. 5,422,097; 1449), Illum (U.S. Patent No. 5,690,954; 1449), Illum (U.S. Patent No. 5,707,644; 1449) and Kublik et al. (Eur. J. Pharm. Biopharm. 39: 192-196, 1993; 1449) essentially for the reasons of record set forth in Paper No. 12.

Applicant's arguments, filed 4/15/03 (Paper No. 13), have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant acknowledges that Igari teaches a pharmaceutically base or vehicle comprising polyvinyl pyrrolidine, hydroxymethyl cellulose, hydroxypropyl, cellulose, chitosan, collagen, sodium alignaite, gelatin, hyaluranoic acid, polyglerin fatty acide esters, or sucrose fatty acid esters (see column 9, lines 8-39) but then argues that Igari does not teach or suggest a liquid formulation comprising chitosan, nor specifically teaches a preparation of microspheres comprising starch, chitosan, gelatin, hyaluronic acid, alginate or gellan in which ICAM-1 has been incorporated.

Applicant acknowledges that Greve teaches a water soluble preparation of human rhinovirus major receptors that reduces the viral infectivity, but then argues that Greve does not teach that preparation can be formulated into any type of pharmaceutical compositions, nor demonstrate any in vivo use of the preparation.

Applicant argues that Wegner is designed for delivery of ICAM-1 to lung endothelia and not to the nasal cavity and does not teach the use of ICAM-1 with microspheres formulated from chitosan, gelatin, hyaluronic acid, alginate and gellan.

Applicant acknowledges that Gwaltney teaches composition which prevent the attachment of rhinovirus to nasal cells, including ICAM-1, but argues that Gwaltney does not teach the use of microspheres and liquid formulations comprising chitosan.

Applicant acknowledges that Illum '954 and Illum-644 teach drug delivery composition comprising starch, gelatin, dextran, collagen and gellan but these references do not teach composition comprising ICAM-1.

Applicant acknowledges that Kublik teach drug compositions for nasal applications comprising gellan and hydroxymethylcellulose but does not teach chitosan nor ICAM-1.

Applicant asserts that the present invention addressing the difficulty in administering an active agent to the nasal cavity.

Applicant asserts that the combinations of the references do not teach nor suggest each element of the claimed invention, including a liquid formulation comprising chitosan, a composition comprising an effective amount of ICAM-1 and ICAM-1 in a concentration of between 0.02-20% by weight per volume.

Once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case the teachings of references are clearly drawn to providing the HRV receptor or ICAM-1 to inhibit rhinovirus attachment and infectivity, including providing ICAM-1 to those areas susceptible to infection by rhinovirus (e.g. see Igari and Greve).

In addition, all of the references provide for appropriate pharmaceutical compositions comprising an active agent and

teach the delivery of compositions comprising ICAM-1 (column 5, line 4), chitosan, gelatin, microspheres, polymeric materials for nasal delivery (see Igari, see entire document, including Abstract, Summary of the Invention, Description of the Preferred Embodiments, columns 7-12, particularly columns 9-10, for example);

teach the use of the HRV receptor or ICAM-1 to inhibit rhinovirus attachment and infectivity, including providing ICAM-1 to those areas susceptible to infection by rhinovirus such as intranasal sprays (see Greve, see entire document, including Summary of the Invention, Description of the Preferred Embodiments, column 4, paragraph 2, for example);

teach delivering ICAM-derived antagonists, including controlled release preparations and polymeric materials (see Wegner, see entire document, including Detailed Description of the Preferred Embodiments, including Administration or the Compositions of the Present Invention on columns 15-16);

teach the use of antiviral ICAM-1 (column 10) including preparation of such antiviral agents for intranasal delivery (see Gwaltney, see entire document, particularly Description of the Preferred Embodiments, including columns 11-12, overlapping paragraph); and

teach various bioadhesive formulations encompassed by the claimed invention for drug delivery to the nasal cavity, as well as the various considerations of mixing said bioadhesive materials with a wide variety of active drugs to increase their bioavailability upon administration (see entire documents of Illum '954, Illum '644 and Kublik et al.).

Furthermore, and for example, Illum ('954) teaches that the bioadhesive formulations and delivery systems provide for greater bioavailability of the active drug and that certain formulations are due to the greater retention of the delivery system in the nasal cavity (for example, see column 4, paragraphs 1-4; column 6, paragraph 2; column 8, paragraphs 5-6). Also, Illum ('954) teaches various Examples of concentrations, including 0.5, 2, 4, and 5% w/v Rose bengal (see columns 7-8, overlapping paragraph

In addition as pointed out previously, Illum ('644) teaches that the amount of drug that can be carried by the microspheres is termed the loading capacity, which is determined by the physico-chemical properties of the drug molecule an in particular its size and affinity for the particle matrix (see column 6, paragraph 3). It is known that for many peptides and proteins the amount of drug substance to be administered for a resultant therapeutic effect will be of the order of a few micrograms or less.

Given the teaching of the prior art including the motivation and expectation of success in providing an antiviral effective amount ICAM-1 to the nasal cavity; it would have been obvious and expected that the various w/v concentrations encompassed by the claims would have been provided in inhibiting rhinovirus attachment and infectivity based on the needs of the patient and the nature of the infection by the ordinary artisan at the time the invention was made. The prior art teaches the various bioadhesive materials encompassed by the claimed invention for the purposes of increasing the bioavailability of active substances. Also, Illum ('954) teach an example of various concentrations of an active substance in polymeric bioadhesive materials that read on the claimed limitations, providing evidence that various concentrations of active ingredients would have been expected at the time the invention was made.

Also, it is noted that where the general condition of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See In re Aller, 105 USPQ 233, 235, (CCPA 1955). See MPEP 2144.05.

Further, a particular parameter must first be recognized as a result-effective variable, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. See In re Antoine, 195 USPQ 6 (CCPA 1977). See MPEP 2144.05.

The prior art clearly provided sufficient motivation and expectation of success of administering an antiviral effective amount of ICAM-1 to the nasal cavity to treat rhinovirus infections and combining ICAM-1 with formulations comprising microspheres and/or the claimed bioadhesives would have been expected and desired formulations to provide antiviral agents such as ICAM-1 to the nasal cavity at the time the invention was made by the ordinary artisan. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

Here, the prior art teaches providing ICAM-1 to combat rhinovirus infections, including intranasal administration and the use of polymeric compositions. In addition, the prior art teaches the various bioadhesive materials encompassed by the claimed invention, including their use with a wide variety of active drugs to achieve increase bioavailability of said active drugs. As pointed out above, Illum ('644) teaches that the amount of drug that can be carried by the microspheres is termed the loading capacity, which is determined by the physico-chemical properties of the drug molecule an in particular its size and affinity for the particle matrix (see column 6, paragraph 3). Therefore, the claimed limitations of formulations of ICAM-1 with bioadhesive materials were within the purview and expectation of the ordinary artisan at the time the invention was made to provide an increased bioavailability of an antiviral effective amount of ICAM-1 intra nasally.

One of ordinary skill in the art at the time the invention was made would have been motivated to provide ICAM-1 with a bioadhesive, including those encompassed by the claimed invention to increase the bioavailability of ICAM-1 in order to inhibit rhinovirus attachment and infectivity. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014..

Phillip Gambel

Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
June 25, 2003